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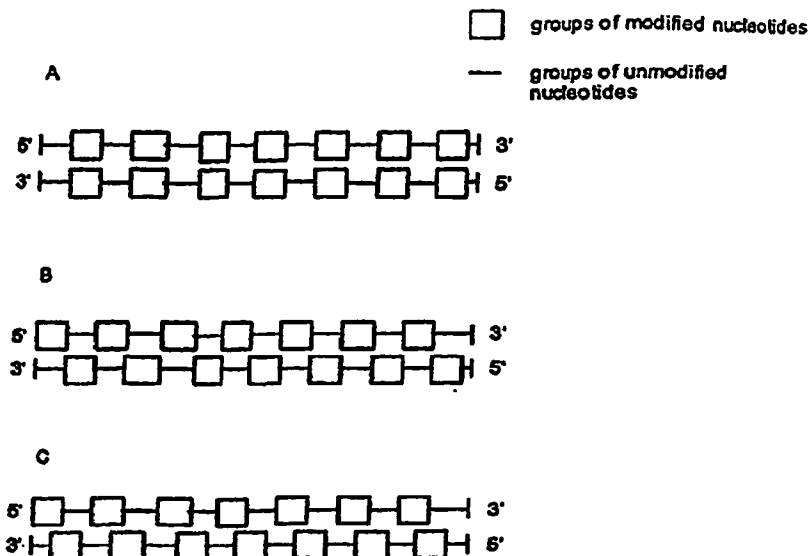
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(54) Title: FURTHER NOVEL FORMS OF INTERFERING RNA MOLECULES



(57) Abstract: The present invention is related to a ribonucleic acid comprising a double stranded structure whereby the double-stranded structure comprises a first strand and a second strand, whereby the first strand comprises a first stretch of contiguous nucleotides and whereby said first stretch is at least partially complementary to a target nucleic acid, and the second strand comprises a second stretch of contiguous nucleotides whereby said second stretch is at least partially identical to a target nucleic acid, and whereby the double stranded structure is blunt ended.



— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*

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INTERNATIONAL SEARCH REPORT

International Application No.

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A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C12N15/11 C07H21/00 A61K31/713 C12Q1/68 A01K67/027
C12N5/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C12N C07H A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BIOSIS, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	PARRISH S ET AL: "Functional anatomy of a dsRNA trigger: Differential requirement for the two trigger strands in RNA interference" MOLECULAR CELL, vol. 6, no. 5, November 2000 (2000-11), pages 1077-1087, XP002226298 ISSN: 1097-2765 page 1081, right-hand column; figure 5 page 1084, left-hand column, paragraph 2	1-5, 9-13,26, 32,42, 44,46
Y		1-46
Y	WO 02/055693 A (RIBOPHARMA AG ; ROST SYLVIA (DE); KREUTZER ROLAND (DE); LIMMER STEPHAN) 18 July 2002 (2002-07-18) the whole document	1-46
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☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

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- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *Z* document member of the same patent family

Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International Application No
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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97/41141 A (UNIV JEFFERSON) 6 November 1997 (1997-11-06) page 12 - page 15, paragraph D. claims; figures	1-3, 5, 9, 26, 32, 33, 36, 37, 40-46
A	WO 95/13834 A (GIACHETTI CHRISTINA ; GENTA INC (US); REYNOLDS MARK A (US); ARNOLD LYL) 26 May 1995 (1995-05-26) page 10, line 31 - page 12 page 21, line 29 - page 30 examples 17A, 35, 44	1-46
A	WO 02/44321 A (MAX PLANCK GESELLSCHAFT ; TUSCHL THOMAS (DE); ELBASHIR SAYDA (DE); LEN) 6 June 2002 (2002-06-06) page 4 - page 14 page 46, paragraph 3.2.4 page 49, paragraph 3.4 claims; figures	1-46
A	WO 00/44895 A (KREUTZER ROLAND ; LIMMER STEPHAN (DE)) 3 August 2000 (2000-08-03) cited in the application	
A	STERNBERGER M ET AL: "GeneBlocs are powerful tools to study and delineate signal transduction processes that regulate cell growth and transformation" ANTISENSE & NUCLEIC ACID DRUG DEVELOPMENT, vol. 12, no. 3, June 2002 (2002-06), pages 131-143, XP002226299 ISSN: 1087-2906 cited in the application	
P, X	CZAUDERNA FRANK ET AL: "Structural variations and stabilising modifications of synthetic siRNAs in mammalian cells." NUCLEIC ACIDS RESEARCH, vol. 31, no. 11, 1 June 2003 (2003-06-01), pages 2705-2716, XP002270732 ISSN: 0305-1048 the whole document	1-32, 42, 44-46
E	WO 03/070912 A (FOSNAUGH KATHY ; JAMISON SHARON (US); MCSWIGGEN JAMES (US); PAVCO PAME) 28 August 2003 (2003-08-28) page 19 - page 21 page 25, line 20 - page 27, line 10 figures 5-8	1-46

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/08666

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 46 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

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Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 02055693	A	18-07-2002	DE 10100586 C1	11-04-2002
			DE 10160151 A1	26-06-2003
			CA 2432341 A1	18-07-2002
			CA 2432350 A1	18-07-2002
			WO 02055692 A2	18-07-2002
			WO 02055693 A2	18-07-2002
			EP 1349927 A2	08-10-2003
			EP 1352061 A2	15-10-2003
			US 2004001811 A1	01-01-2004
			WO 03033700 A1	24-04-2003
			WO 03035868 A1	01-05-2003
			WO 03035869 A1	01-05-2003
			WO 03035870 A1	01-05-2003
			WO 03035082 A1	01-05-2003
			WO 03035083 A1	01-05-2003
			WO 03035876 A1	01-05-2003
WO 9741141	A	06-11-1997	US 5760012 A	02-06-1998
			AU 708658 B2	12-08-1999
			AU 2822597 A	19-11-1997
			CA 2252762 A1	06-11-1997
			EP 0906328 A1	07-04-1999
			JP 2000509282 T	25-07-2000
			NZ 332297 A	27-03-2000
			WO 9741141 A1	06-11-1997
			US 5888983 A	30-03-1999
WO 9513834	A	26-05-1995	AU 695552 B2	13-08-1998
			AU 1183495 A	06-06-1995
			AU 689182 B2	26-03-1998
			AU 1291695 A	06-06-1995
			CA 2176259 A1	26-05-1995
			CA 2176372 A1	26-05-1995
			EP 0731809 A1	18-09-1996
			EP 0743859 A1	27-11-1996
			IL 128658 A	12-03-2003
			JP 9506248 T	24-06-1997
			JP 9505307 T	27-05-1997
			NZ 276968 A	27-04-1998
			NZ 277617 A	26-01-1998
			TW 390884 B	21-05-2000
			WO 9513834 A1	26-05-1995
			WO 9514031 A1	26-05-1995
			US 6262036 B1	17-07-2001
			US 5837856 A	17-11-1998
			US 5955597 A	21-09-1999
			US 6060456 A	09-05-2000
			AU 678085 B2	15-05-1997
			AU 1181995 A	06-06-1995
			AU 687492 B2	26-02-1998
			AU 1291595 A	06-06-1995
			CA 2176256 A1	26-05-1995
			CA 2176498 A1	26-05-1995
			EP 0729474 A1	04-09-1996
			EP 0735899 A1	09-10-1996
			JP 9507836 T	12-08-1997
			JP 9505306 T	27-05-1997
			NZ 276956 A	27-04-1998

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/08666

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9513834	A	NZ 277616 A	19-12-1997
		WO 9514030 A1	26-05-1995
		WO 9513833 A1	26-05-1995
		US 5986083 A	16-11-1999
		US 6028188 A	22-02-2000
		US 5792615 A	11-08-1998
		AU 2584395 A	16-11-1995
		WO 9528942 A1	02-11-1995
WO 0244321	A 06-06-2002	AU 3574402 A	11-06-2002
		AU 4962201 A	15-10-2001
		CA 2404890 A1	11-10-2001
		CA 2429814 A1	06-06-2002
		CZ 20031839 A3	15-10-2003
		WO 0244321 A2	06-06-2002
		EP 1309726 A2	14-05-2003
		HU 0302557 A2	28-10-2003
		JP 2003529374 T	07-10-2003
		NO 20032464 A	21-07-2003
		WO 0175164 A2	11-10-2001
		US 2003108923 A1	12-06-2003
		US 2002086356 A1	04-07-2002
WO 0044895	A 03-08-2000	DE 19956568 A1	17-08-2000
		AT 222953 T	15-09-2002
		AU 3271300 A	18-08-2000
		CA 2359180 A1	03-08-2000
		WO 0044895 A1	03-08-2000
		DE 10080167 D2	28-02-2002
		DE 50000414 D1	02-10-2002
		EP 1144623 A1	17-10-2001
		EP 1214945 A2	19-06-2002
		ES 2182791 T3	16-03-2003
		JP 2003502012 T	21-01-2003
		ZA 200105909 A	24-07-2002
WO 03070912	A 28-08-2003	US 2003064945 A1	03-04-2003
		US 2003186909 A1	02-10-2003
		US 2003105051 A1	05-06-2003
		US 2003170891 A1	11-09-2003
		WO 03070912 A2	28-08-2003
		WO 02097114 A2	05-12-2002
		WO 03072704 A2	04-09-2003
		WO 03072705 A2	04-09-2003
		WO 03070983 A1	28-08-2003
		WO 03070742 A1	28-08-2003
		WO 03070881 A2	28-08-2003
		WO 03070884 A2	28-08-2003
		WO 03070885 A2	28-08-2003
		WO 03070886 A2	28-08-2003
		WO 03070743 A1	28-08-2003
		WO 03070887 A2	28-08-2003
		WO 03070888 A2	28-08-2003
		WO 03070966 A2	28-08-2003
		WO 03070744 A1	28-08-2003
		WO 03070895 A2	28-08-2003
		WO 03070896 A2	28-08-2003
		WO 03070897 A2	28-08-2003

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/08666

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03070912	A	WO 03070968 A2	28-08-2003
		WO 03070969 A2	28-08-2003
		WO 03070903 A2	28-08-2003
		WO 03070970 A2	28-08-2003
		WO 03070910 A2	28-08-2003
		WO 03074654 A2	12-09-2003
		WO 03070750 A2	28-08-2003
		WO 03070911 A2	28-08-2003
		WO 03070914 A2	28-08-2003
		WO 03070193 A2	28-08-2003
		WO 03070972 A2	28-08-2003
		WO 03070917 A2	28-08-2003
		WO 03070918 A2	28-08-2003
		WO 03070197 A2	28-08-2003
		WO 03102131 A2	11-12-2003
		WO 03106476 A1	24-12-2003
		US 2004006035 A1	08-01-2004
		WO 03072590 A1	04-09-2003
		US 2003206887 A1	06-11-2003
		US 2003190635 A1	09-10-2003